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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,545	04/09/2004	Michael E. Hepperle	MPI03-043P1RNM	1299

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MILLENNIUM PHARMACEUTICALS, INC.
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EXAMINER
ANDERSON, REBECCA L

ART UNIT	PAPER NUMBER
1626	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/821,545

Applicant(s)

HEPPERLE ET AL.

Examiner

Rebecca L. Anderson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 2-7, 19-27 and 30-34 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 28 is/are allowed.
- 6) ☒ Claim(s) 1, 8-15, 17 and 29 is/are rejected.
- 7) ☒ Claim(s) 1, 8, 9, 12, 13 and 16-18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/26/04, 5/30/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-34 are currently pending in the instant application. Claims 2-7, 19-27 and 30-34 are withdrawn from consideration as being for non-elected subject matter. Claims 1, 8-15, 17 and 29 are rejected. Claims 1, 8, 9, 12, 13 and 16-18 are objected.

Election/Restrictions

Applicant's election without traverse of Group I and the further election of the compound of example 40 in the reply filed on 29 January 2007 is acknowledged.

Newly added claims 30-34 are method claims which are part of restricted Group III and are therefore withdrawn from consideration as being for non-elected subject matter.

Therefore, as stated on pages 3 and 4 of the restriction requirement and based upon the election of Group I and the compound of example 40, the elected invention for search and examination is:

The products of the formula I wherein A is a morpholinyl that is substituted by (i), (ii) and (iii) and the products of the formula's III-A; (S)-III-A; (S)-III-A'; (S)-III-A-a; and the products of the formula (IV).

The remaining subject matter of claim 1, 8, 9 and 16-18 that is not drawn to the above elected invention and the subject matter of claims 2-7, 19-27 and 30-34 stands withdrawn under 37 CFR 1.142(b) as being for non-elected subject matter. The remaining compounds which are not within the elected invention, which are independent and distinct from the elected invention and do not have unity with the elected compound and are therefore withdrawn by means of a restriction requirement within the claims are,

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for example, the compounds of the formula I wherein ring A is pyridinyl, pyrimidinyl, piperidinyl, piperazinyl, pyrrolidinyl, pyranyl, tetrahydrofuranyl, cyclohexyl, cyclopentyl or thiomorpholinyl, etc.

The above mentioned withdrawn compounds which are withdrawn from consideration as being for nonelected subject matter differ materially in structure and composition from the compounds of the elected invention. The withdrawn compounds differ from those of the elected invention, such as by pyridinyl, pyrimidinyl, piperidinyl, piperazinyl, pyrrolidinyl, pyranyl, etc. which are chemically recognized to differ in structure and function. This recognized chemical diversity of the compounds can be seen by the various classification of these compounds in the U.S. classification system. Therefore, again, the compounds which are withdrawn from consideration as being for non-elected subject matter differ materially in structure and composition and have been restricted properly as a reference which anticipated but the elected subject matter would not even render obvious the non-elected subject matter.

These withdrawn compounds are independent and distinct from the elected invention and do not have unity with the compound elected and are therefore withdrawn by means of a restriction requirement within the claims.

The restriction requirement is considered proper and is maintained.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied

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with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/461,468 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Specifically, claims 1, 8-18, 28 and 29 are not entitled to the benefit of the prior application as subject matter found in the instant claims does not find support in Application No. 60/461,468. For example, wherein Ring A is a morpholinyl that is substituted by (i), (ii) and (iii) does not find support in the prior-filed application as the prior-filed application only provides support for morpholinyl attached at the 3-position with specific substituents. Additionally, wherein R1 is halo and R3 is cyano also does not find support in the prior-filed application as the prior-filed application does not allow or provide a definition for R1 and R3 as halo or cyano, respectively.

Accordingly, claims 1, 8-18, 28 and 29 are not entitled to the benefit of the prior application.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 26 November 2004 and 30 May 2006 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner. US Patent Application No. 11/390,287 has a line drawn through the citation because there is no patentee or publication date provided. However, an 892 has been provided which cites the pre-grant publication of Application No. 11/390,287 which is Pre-Grant Publication No. 20060166978. Additionally, on 15 February 2007, Karoline K.M. Shair confirmed that the 1449 filed 30 May 2006 is only 1 page and not 2 pages.

Claim Objections

Claims 1, 8, 9 and 16-18 are objected to as containing non-elected subject matter. Claims 1, 8, 9 and 16-18 presented drawn solely to the elected invention identified supra as the elected invention for search and examination would overcome this objection.

Claims 12 and 13 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, specifically claim 11. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically, claim 11, which depends from claim 10 defines R12 as hydrogen or an amino acid side chain. Claims 12 and 13 define R12 as hydrogen, C1-6aliphatic, substituted or unsubstituted phenyl, or substituted or unsubstituted benzyl. This definition of R12 fails to further limit claim 11 as claim 11 does not allow for R12 to be

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C1-6aliphatic, substituted or unsubstituted phenyl, or substituted or unsubstituted benzyl. See pages 15 and 16 of the specification which have "amino acid side chain" as a different substituent than C1-6 aliphatic, phenyl or benzyl.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-13, 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the terms "having", used in the definitions of the compounds in the claimed process renders the products indefinite as forms of the term "having" can be considered open ended language and is therefore including additional subject matter in the compounds of the claims that is not described in the instant specification and is not particularly pointed out or distinctly claimed. A definition of a chemical compound cannot be open-ended, but must be claimed with precision. For example, an alkyl group having 1 to 6 carbon atoms can be read to include additional atoms and groups other than carbon and alkyl, however, the identity of the additional atoms or groups and how to determine the identity of the additional atoms or groups is not pointed out or distinctly claimed. It is suggested that the term "having" be deleted from the claims and replaced with, for example -of-, see for example, the following phrase: "A compound of the formula".

Claims 1, 8-11, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

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which applicant regards as the invention. Specifically, the phrase “amino acid side chain” renders the claims indefinite as it is unclear what substituents are considered “amino acid side chains”. Pages 15 of the specification states that R12 can be hydrogen, C1-6aliphatic, substituted or unsubstituted phenyl, substituted or unsubstituted benzyl or an amino acid side chain. Therefore, hydrogen, C1-6aliphatic, phenyl and benzyl are not considered amino acid side chains as they are defined as different values for R12. Amino acids can be natural and unnatural amino acids. It is unclear what side chains are considered amino acid side chains since hydrogen C1-6aliphatic, phenyl and benzyl are not considered amino acid side chains. It is unclear what are “amino acid side chains” as there is no guidance on how to determine if a substituent is an “amino acid side chain”. Additionally, while page 16 states that amino acid side chains are particularly side chains of a natural amino acid, this still does not provide a definition for what these side chains are and are not. What side chains are considered “amino acid side chains” and how is one to determine what side chains are and are not amino acid side chains.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims must, under modern claim practice, stand alone to define an invention, *Ex parte Fressola*, 27 USPQ 2d 1608 (1993). The instant claim does not provide what (S)—IV is and does not stand alone to define the invention as it is unclear what limitations are instituted for formula IV of claim 28 with the limitation of claim 29 as it is unclear what (S)-IV is. Does (S)-IV narrow the definitions for the

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variables of formula IV or does (S)-IV define a specific configuration for formula IV?

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical; but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 8-15 and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 11/101998. Although the conflicting claims are not identical, they are not patentably distinct from each other because conflicting claims 1-19 provide compounds and pharmaceutical compositions which overlap with applicants instantly claimed elected invention. Conflicting claims 1-3 provide products which overlap with applicants' instantly claimed elected invention. Conflicting claims 4-16 provide preferences towards applicants' instantly claimed elected invention such as wherein G is a nitrogen-containing N-linked heterocyclyl ring (conflicting claims 4 and 5); wherein Q is CH₂ (conflicting claims 6-9); wherein the compound is (S) (claims 10-13); wherein G is piperidinyl, piperazinyl, morpholinyl, pyrrolidinyl (conflicting claim 14); wherein G is N-piperidinyl, N-piperazinyl, N-morpholinyl or N-pyrrolidinyl (conflicting claim 15); and wherein R_b is methyl (conflicting claim 16). Conflicting claim 19 provides pharmaceutical compositions. Conflicting claims 17 and 18 provide species which anticipate applicants instantly claimed elected invention, such as, for example, compound 65 which corresponds to applicants' instant elected invention wherein Ring A is morpholinyl; R₁ is hydrogen; R₂ is halo; R₃ is hydrogen; and morpholinyl is substituted by -W-G and 2 R_b wherein R_b is C₁₋₆ aliphatic; W is Z-Q-C(O) wherein Q is CH₂; and G is N-piperidinyl.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1, 8, 9 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castro et al. (C1 reference on 1449 and U reference on 892).

Determining the scope and contents of the prior art

Castro et al discloses the compound 35 and registry no. 590398-98-4 useful to inhibit IKK for the treatment of certain inflammatory diseases (pages 2419 and 2421 and abstract).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art provides an unsubstituted ring A wherein ring A of the instant claims is substituted by at least one of C(R₉)₃, W-G or G, wherein C(R₉)₃ can be methyl. Therefore, the difference between the instant claims and the prior art can be a hydrogen versus a methyl on the morpholine ring.

Resolving the level or ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare compounds of applicants instant elected invention when faced with the prior art of Castro et al., which discloses compound 35 and registry no.590398-98-4 which are useful as inhibitors of IKK for the treatment of certain inflammatory diseases. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation

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to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (ie., inhibitors of IKK).

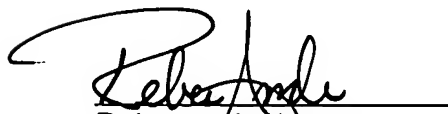
Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Rebecca Anderson
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Art Unit 1626, Group 1620
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16 February 2007